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The Crystal Structure and Conformation of 2′,3′-*O*-Isopropylideneadenosine: The Co-existence of a Planar and a Puckered Ribofuranose Ring

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2′,3′-*O*-Isopropylideneadenosine (IPLA) is a nucleoside in which the ribofuranose group is cyclized at the O(2′) and O(3′) atoms. IPLA crystallizes in the orthorhombic space group $P2_12_12_1$ with cell constants a = 20·957 (8), b = 17·134 (7), c = 7·940 (3) Å. There are two independent molecules in the asymmetric unit. The intensities of 2663 independent reflections were measured on a Picker FACS-I diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares techniques to a conventional R of 0·063. There are substantial differences in conformation between the two independent molecules. The ribofuranose ring of molecule A is essentially planar and the dioxolane ring assumes the C(6′) *endo*, O(2′) *exo* pucker. The conformation about the C(4′)—C(5′) bond is *gauche*⁺ (Ψ = 53·6°). In contrast, the ribofuranose group of molecule B exhibits the unusual $_3T^4$ twist while the dioxolane ring is puckered in the C(3′) *endo*, O(3′) *exo* mode. The conformation about the C(4′)—C(5′) bond is *trans* (Ψ = 174·5°). Both nucleosides are observed in the *anti* glycosyl conformation, χ = 10·5 and 15·9° in molecules A and B, respectively. The molecular packing is dominated by the self-pairing of the adenine bases which forms a hydrogen-bonding network in the *ac* plane involving the atoms N(1), N(6) and N(7) of the adenine rings. The bases of molecules A and B are partially overlapped and there are close-contacts between the ribose ring oxygen of molecule B and the imidazole moiety of the screw-related molecule A.

Introduction

2′,3′-*O*-Isopropylideneadenosine (IPLA) is a nucleoside in which the ribose ring is cyclized at the O(2′) and O(3′) atoms. This modification is expected to constrain the conformational flexibility of the furanose ring. To date, only a limited number of crystal structures have been reported of 2′,3′-*O*-isopropylidene nucleosides and their derivatives, *viz.* 8-bromo-2′,3′-*O*-isopropylideneinosine (Fujii, Fujiwara & Tomita, 1976), 2-methyl-8-bromo-2′,3′-*O*-isopropylideneinosine (Matsuda, Tomita, Fujiwara, Fujii & Ikehara, 1974), 5′,2-*O*-cyclo-2′,3′-*O*-isopropylideneuridine (Manor, Saenger, Davis, Jankowski & Rabczenko, 1974) and a 2′,3′-*O*-isopropylideneerythrofuranoside (Liebich, 1976). Among these, IPLA is the only compound with an unmodified base. A related structure, 2′,3′-*O*-methoxymethyleneuridine (de Kok, Romers, de Leeuw, Altona & van Boom, 1977), has also been recently elucidated.

We have undertaken the structural analysis of IPLA in order to investigate the effect of chemical modifications in the furanose ring on the overall conformation of nucleosides.

Experimental

A sample of IPLA, kindly provided by Dr P. Hart of the Department of Pharmacy, was crystallized by slow evaporation from 50% aqueous ethanol to form thin needles elongated along the c axis. The pertinent crystal data are given in Table 1. Unit-cell parameters were refined by a least-squares method using the orientation angles θ, χ and φ of 12 reflections, 40° ≤ 2θ ≤ 60° (Cu $K\alpha$ radiation), which were automatically centered on a Picker FACS-1 automated diffractometer.

The intensity data were measured with Ni-filtered Cu $K\alpha$ radiation by a θ–2θ scan at a rate of 2° min^{-1} with background counts of 10 s taken at each scan limit. The intensities of three reflections were monitored at regular intervals throughout the data collection and were not found to vary. Of a total of 2663 reflections measured to a 2θ limit of 127°, 2031 had intensities greater than $1{\cdot}5\sigma(I)$ and were used in the structure analysis. The data were corrected for Lorentz and polarization effects but, due to the small size of the

Table 1. *Crystal data*

Formula	$C_{13}H_{17}N_5O_4$	V	2851 Å^3
M_r	307·3	D_m	1·432 g cm^{-3} (flotation in cyclohexane/$CHCl_3$)
Space group	$P2_12_12_1$		
a	20·957 (8) Å	D_x	1·430
b	17·134 (7)	Z	8
c	7·940 (3)	μ	9·26 cm^{-1}

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crystal (0·15 × 0·15 × 0·33 mm) and the low value for the absorption coefficient, no absorption correction was applied.

Structure determination and refinement

The structure was solved by application of the multi-solution tangent formula technique using the computer program *MULTAN* (Main, Germain & Woolfson, 1970). The 308 highest normalized structure factors with $|E| \geq 1{\cdot}5$ were used to generate 2000 $\sum_2$ relationships. Origin- and enantiomorph-defining reflections and those constituting the starting set were chosen automatically by the program, but, due to the lack of relationships involving strong reflections of the type *h*0*l*, convergence could not be attained. Examination of the set of $\sum_2$ relationships suggested an alternative choice of origin- and enantiomorph-defining reflections which led to a successful phase determination. The phases of the four reflections of the starting set were varied to yield 32 solutions, all of which were submitted to tangent refinement. The correct solution had the highest figure of merit, 1·04, and the lowest Karle residual, *R*(*E*), of 0·36. A three-dimensional Fourier synthesis using the 308 normalized structure factors revealed the positions of all the non-hydrogen atoms in the asymmetric unit with the exception of the isopropylidene carbon atoms. These latter atoms were subsequently located in a difference Fourier synthesis using all observed data and phases derived from the partial structure.

Table 2. *Positional parameters* (×10⁴) *of non-hydrogen atoms in* 2′,3′-*O-isopropylideneadenosine*

Standard deviations in parentheses refer to the least significant digit(s).

	x	*y*	*z*
C(8′)*A*	7891 (4)	3265 (8)	−1177 (17)
C(7′)*A*	7574 (4)	4608 (6)	−740 (13)
C(6′)*A*	7414 (2)	3767 (4)	−373 (8)
O(5′)*A*	5941 (2)	3570 (4)	4851 (7)
C(5′)*A*	6432 (3)	3001 (5)	4731 (9)
C(4′)*A*	6595 (2)	2924 (4)	2894 (7)
O(3′)*A*	7390 (2)	3649 (3)	1369 (6)
C(3′)*A*	6765 (3)	3675 (4)	1958 (7)
O(2′)*A*	6794 (2)	3579 (4)	−945 (5)
C(2′)*A*	6349 (3)	3691 (4)	405 (7)
O(1′)*A*	6074 (2)	2566 (2)	1961 (5)
C(1′)*A*	5914 (2)	2967 (3)	536 (7)
N(9)*A*	5234 (2)	3183 (6)	602 (6)
C(8)*A*	4821 (3)	3134 (4)	1915 (7)
N(7)*A*	4233 (2)	3317 (3)	1551 (6)
N(6)*A*	3176 (2)	3867 (3)	−922 (6)
C(6)*A*	3785 (2)	3750 (3)	−1289 (6)
C(5)*A*	4255 (2)	3491 (3)	−135 (7)
C(4)*A*	4873 (2)	3411 (3)	−756 (7)
N(3)*A*	5078 (2)	3547 (3)	−2324 (6)
C(2)*A*	4588 (3)	3777 (4)	−3320 (7)
N(1)*A*	3977 (2)	3885 (3)	−2912 (6)
C(8′)*B*	−1090 (4)	4446 (5)	2637 (10)
C(7′)*B*	−1341 (3)	3118 (5)	3905 (10)
C(6′)*B*	−930 (3)	3854 (4)	3957 (8)
O(5′)*B*	439 (3)	4610 (4)	10159 (7)
C(5′)*B*	163 (3)	4042 (4)	9213 (9)
C(4′)*B*	−207 (3)	4456 (4)	7808 (8)
O(3′)*B*	−961 (2)	4219 (2)	5589 (6)
C(3′)*B*	−477 (2)	3872 (3)	6597 (8)
O(2′)*B*	−272 (2)	3616 (3)	3775 (5)
C(2′)*B*	48 (2)	3733 (3)	5309 (9)
O(1′)*B*	225 (2)	4933 (3)	6765 (5)
C(1′)*B*	428 (2)	4497 (3)	5388 (7)
N(9)*B*	1125 (2)	4370 (3)	5506 (6)
C(8)*B*	1519 (2)	4453 (4)	6804 (7)
N(7)*B*	2121 (2)	4290 (3)	6503 (6)
N(6)*B*	3210 (2)	3802 (4)	4067 (6)
C(6)*B*	2597 (2)	3874 (4)	3680 (6)
C(5)*B*	2111 (2)	4088 (4)	4813 (7)
C(4)*B*	1498 (2)	4134 (3)	4160 (7)
N(3)*B*	1311 (2)	3990 (3)	2602 (6)
C(2)*B*	1809 (3)	3783 (5)	1637 (7)
N(1)*B*	2417 (2)	3711 (2)	2058 (7)

The structure was submitted to three cycles of full-matrix least-squares refinement of *F* with isotropic temperature factors and the reflections given unit

Table 3. *Positional parameters* (×10³) *and isotropic temperature factors of hydrogen atoms*

Parameters showing no standard deviations have not been refined by least squares.

	x	*y*	*z*	*B* (Å²)
H(2)*A*	477 (3)	397 (4)	−457 (9)	7·1 (1·8)
H(6)*A*1	293 (2)	404 (3)	−155 (6)	3·0 (1·0)
H(6)*A*2	304 (4)	372 (5)	−9 (11)	9·5 (2·4)
H(8)*A*	495 (3)	300 (3)	308 (7)	5·0 (1·4)
H(1′)*A*	593 (3)	275 (4)	−85 (8)	5·9 (1·5)
H(2′)*A*	602 (3)	421 (4)	51 (9)	7·2 (1·8)
H(3′)*A*	677 (4)	411 (5)	273 (10)	8·9 (2·2)
H(4′)*A*	695 (4)	246 (4)	301 (8)	6·0 (1·6)
H(5′)*A*1	628	246	516	6·0
H(5′)*A*2	684	315	538	6·0
H(O5′)*A*	570	360	594	8·0
H(7′)*A*1	804	470	−59	8·0
H(7′)*A*2	742	475	−192	8·0
H(7′)*A*3	732	495	12	8·0
H(8′)*A*1	793	276	−47	8·0
H(8′)*A*2	775	313	−236	8·0
H(3′)*A*3	832	353	−118	8·0
H(8)*B*	140 (3)	457 (3)	781 (8)	5·1 (1·5)
H(6)*B*1	331 (3)	384 (4)	527 (9)	6·5 (1·7)
H(6)*B*2	348 (2)	363 (2)	325 (6)	2·4 (1·0)
H(2)*B*	165 (3)	363 (3)	69 (9)	5·1 (1·4)
H(1′)*B*	28 (2)	478 (3)	421 (6)	2·9 (1·0)
H(2′)*B*	29 (3)	326 (3)	563 (8)	4·7 (1·3)
H(3′)*B*	−58 (3)	338 (3)	696 (7)	4·5 (1·3)
H(4′)*B*	−56 (2)	488 (3)	842 (7)	3·6 (1·1)
H(5′)*B*1	50	370	868	6·0
H(5′)*B*2	−15	372	991	6·0
H(O5′)*B*	64 (5)	418 (6)	1110 (14)	13·2 (3·4)
H(7′)*B*1	−185	336	397	8·0
H(7′)*B*2	−130	279	289	8·0
H(7′)*B*3	−125	274	471	8·0
H(8′)*B*1	−77	490	270	8·0
H(8′)*B*2	−107	418	132	8·0
H(8′)*B*3	−160	448	304	8·0

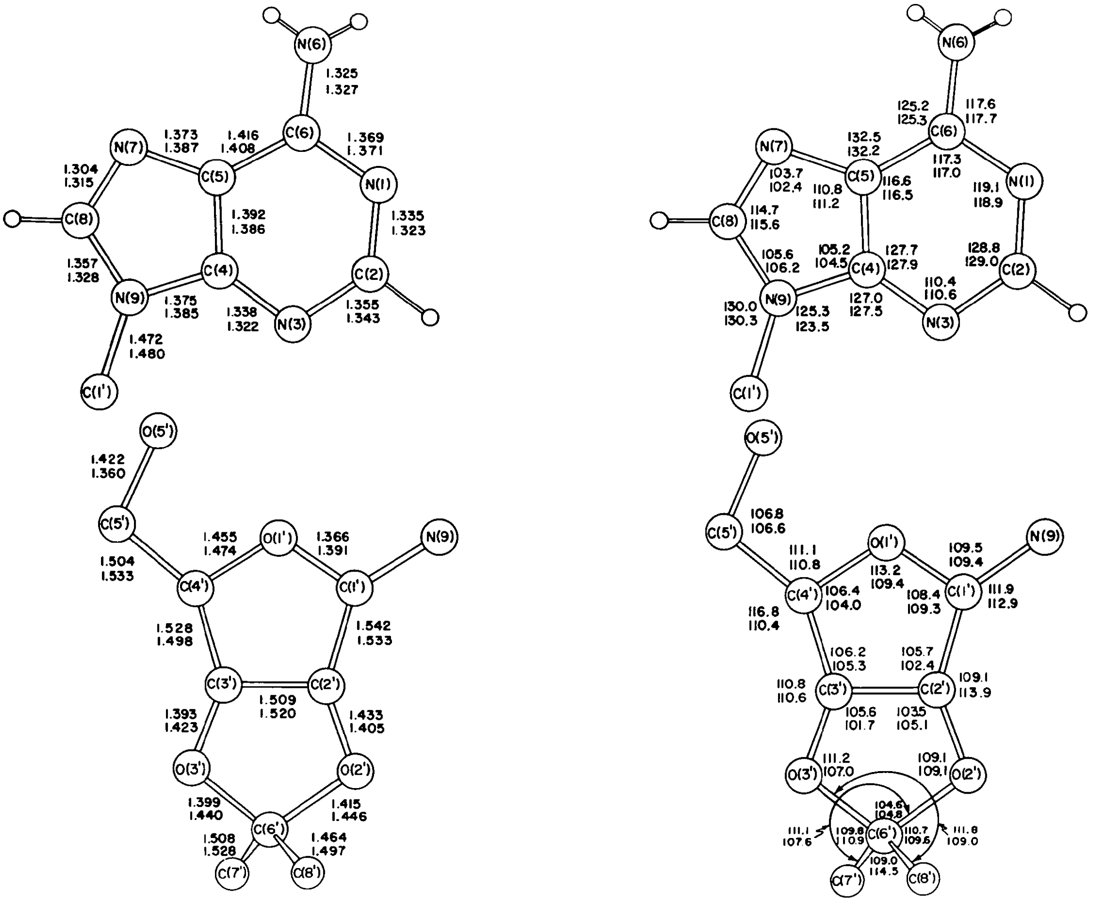

Fig. 1. Bond lengths, bond angles, and atom numbering in IPLA. The upper numbers are for molecule *A* and lower numbers for molecule *B*. The estimated standard deviations in bond lengths are as follows: σ (bond) = 0·007–0·008 Å, σ (angle) = 0·4–0·5°.

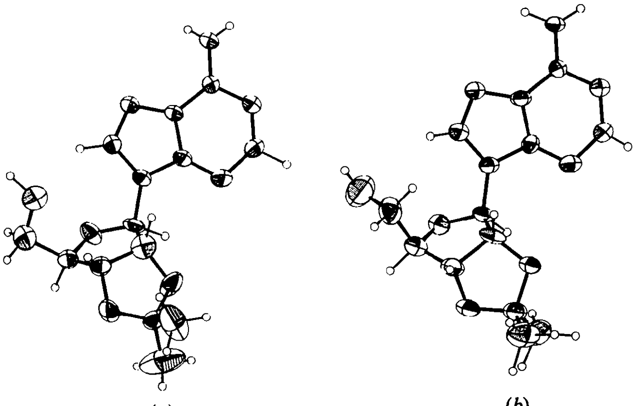
(*a*) (*b*)

Fig. 2. *ORTEP* drawing showing 50% probability ellipsoids of the non-hydrogen atoms of IPLA. Hydrogen atoms are depicted by spheres of an arbitrary diameter. (*a*) molecule *A*; (*b*) molecule *B*.

weight. The *R* index $[R = (\sum ||F_o| - |F_c||)/\sum |F_o|]$ dropped from the initial value of 0·27 to 0·19. The reflections 040, 080, 150, 140, 261, 410 and 460, considered affected by secondary extinction, were given zero weight in subsequent refinement cycles with anisotropic temperature factors. The molecules *A* and *B* were refined in alternate cycles and a modified Hughes (1941) weighting scheme, where $1/\sqrt{w} = 1$ for $|F| < 16$ and $1/\sqrt{w} = 16/|F|$ for $|F| \geq 16$, was applied. After two cycles of anisotropic least-squares refinement, the majority of the hydrogen atoms were located in a difference Fourier synthesis. The electron density corresponding to the methyl, C(5′) and O(5′) hydroxyl hydrogen atoms of molecule *A*, and the methyl and C(5′) hydrogen atoms of molecule *B* was diffuse. Consequently, the positions of these atoms were fixed by geometric criteria. Hydrogen atoms were assigned isotropic thermal parameters equal to those of the non-hydrogen atoms to which they were bound. Those hydrogen atoms not fixed were subjected to four cycles of isotropic least-squares refinement which reduced the *R* value to 0·07. A difference Fourier synthesis calculated at this stage revealed two peaks of low density ($\rho \simeq 0{\cdot}5$ e Å^{-3}) within 0·5 Å of the O(5′)*A* atom and distributed on either side of it. These were provisionally considered as disordered sites of minor occupancy (0·05 for each) and submitted to isotropic refinement which resulted in the increase of thermal parameters for the minor sites to unreasonable values. Therefore, the minor sites were disregarded and the O(5′) *A* atom was given full occupancy at the original position in further calculations. Three final cycles of anisotropic refinement of the non-hydrogen atoms reduced the *R* index to 0·063. There were no significant residual peaks in the final difference Fourier maps. The average and maximum values of the shift/σ for the atomic parameters after refinement were 0·03 and 0·09, respectively, for the non-hydrogen atoms and 0·22 and 0·47, respectively, for the hydrogen atoms.

The scattering factors used for O, N and C atoms were taken from Cromer & Waber (1965) and those for H were from Stewart, Davidson & Simpson (1965).

Results and discussion

The final positional and, for H, thermal parameters for all atoms are given in Tables 2 and 3.* The bond distances and bond angles involving non-hydrogen atoms are shown in Fig. 1. The distances and angles involving the hydrogen atoms are within the usual ranges. Fig. 2 is an *ORTEP* drawing (Johnson, 1965) illustrating the 50% probability ellipsoids for the non-hydrogen atoms and the overall molecular conformations of the two molecules of the asymmetric unit.

Molecular conformation and geometry

Glycosyl conformation

Both molecules of IPLA (planar and puckered) adopt the *anti* conformation about the glycosyl bond (Table 4). The relative importance of the *anti* conformation in the 2′,3′-cyclic purine nucleosides cannot be inferred from the limited solid-state data available. Analysis of the intramolecular nuclear Overhauser effects in IPLA (Schirmer, Davis, Noggle & Hart, 1972), assuming a planar or C(3′) *endo* puckered sugar, has indicated that the *syn* conformer is predominant in solution. Theoretical energy calculations have not been performed on isopropylidene systems but potential-energy calculations (Yathindra & Sundaralingam, 1974) and quantum-mechanical calculations (Saran, Berthod & Pullman, 1973) on the analogous 2′,3′-cyclic purine nucleoside phosphates in which the ribose ring is unpuckered reveal a preference for the *syn* conformation. These results are far from complete, but, taken together with studies of molecular models, clearly indicate that both the *syn* and *anti* conformations are nearly equally favored for isopropylidene purine nucleosides as is also the case with the common purine nucleosides (Sundaralingam, 1973).

Conformation of the fused furan-dioxolane bicyclic group

The conformational parameters for the two independent molecules are summarized in Table 4. The dioxolane ring is described in terms of the pseudorotation model (Altona & Sundaralingam, 1972) and

Table 4. *Conformational parameters* (°) *for* 2′,3′-*O-isopropylideneadenosine*

		Molecule *A*	Molecule *B*		Molecule *A*	Molecule *B*
Glycosyl torsion angle	χ	10·5 (*anti*)	15·9 (*anti*)			
Endocyclic ring torsion angles						
		Ribofuranose			Dioxolane	
	τ_0*	−0·6	8·9	λ_0†	−21·3	−27·9
	τ_1	−2·0	10·7	λ_1	9·1	35·2
	τ_2	3·5	−25·6	λ_2	6·5	−29·7
	τ_3	−3·9	31·4	λ_3	−19·8	13·5
	τ_4	2·8	−25·3	λ_4	25·5	7·9
Pseudorotation parameters						
Phase angle of pseudorotation	**P**	–	215·3	$\mathbf{P}_\lambda$	75·2	147·8
Maximum amplitude of pseudorotation	τ_m	–	31·5	λ_m	25·4	35·1
Mode of ring pucker		planar	${}_3T^4$		${}^{C(6')}T_{O(2')}$	${}^{C(3')}T_{O(3')}$
Conformation about C(4′)—C(5′)						
C(3′)—C(4′)—C(5′)—O(5′)	ψ	53·6 (*gauche*$^+$)	174·5 (*trans*)			
O(1′)—C(4′)—C(5′)—O(5′)		−58·7	59·8			

* τ angles are endocyclic ribofuranose torsion angles with rotations about: τ_0, O(1′)—C(1′); τ_1, C(1′)—C(2′); τ_2, C(2′)—C(3′); τ_3, C(3′)—C(4′); τ_4, C(4′)—O(1′).

† λ angles are endocyclic dioxolane torsion angles with rotations about: λ_0, C(6′)—O(3′); λ_1, O(3′)—C(3′); λ_2, C(3′)—C(2′); λ_3, C(2′)—O(2′); λ_4, O(2′)—C(6′).

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* Lists of structure factors and anisotropic thermal parameters of the nonhydrogen atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33508 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

the convention adopted for the endocyclic torsion angles is similar to that applied for the furanose moiety where $\theta_0 = \lambda_2$, $\theta_1 = \lambda_3$, $\theta_2 = \lambda_4$, $\theta_3 = \lambda_0$, $\theta_4 = \lambda_1$ (Sprang, 1977). We note that a similar convention has been adopted by de Kok, Romers, de Leeuw, Altona & van Boom (1977). For both ribofuranose and dioxolane rings, '*endo*' is defined as a displacement from the bicyclic surface in the direction of the C(5′) atom with respect to least-squares planes through the dioxolane or furanose ring.

The bicyclic conformations of molecules *A* and *B* differ considerably as is illustrated in Fig. 3. The ribose ring of molecule *A* is nearly planar, although it displays a very slight C(3′) *endo* (^3E) twist. The C(3′) atom is displaced by 0·060 Å from the least-squares plane through the remaining four atoms of the furan ring. The dioxolane ring is puckered C(6′) *endo*, O(2′) *exo*. Molecule *A* adopts the common *gauche*$^+$ conformation about the C(4′)—C(5′) bond.

In molecule *B*, the ribofuranose exhibits the unusual C(3′) *exo*, C(4′) *endo* ($_3T^4$) twist in which the atoms C(3′)*B* and C(4′)*B* are displaced by 0·277 and 0·215 Å on opposite sides from the plane of the three remaining atoms of the furanose ring. The dioxolane ring assumes a C(3′) *endo*, O(3′) *exo* conformation in which C(3′)*B* and O(3′)*B* show respective displacements of 0·342 and 0·190 Å from the plane of the remaining three dioxolane ring atoms. The respective pseudorotation parameters are given in Table 4. Unlike molecule *A*, the conformation about the C(4′)—C(5′) bond is *trans*. The results of IPLA taken in conjunction with the available data on other 2′,3′-isopropylidene nucleosides and the related 2′,3′-cyclic nucleoside phosphates indicate that the furanose moiety in these systems can adopt a variety of conformations. It is also evident that the conformations of the fused furan and dioxolane rings are coupled. These aspects are explored in greater detail elsewhere (Sprang & Sundaralingam, 1978*a*).

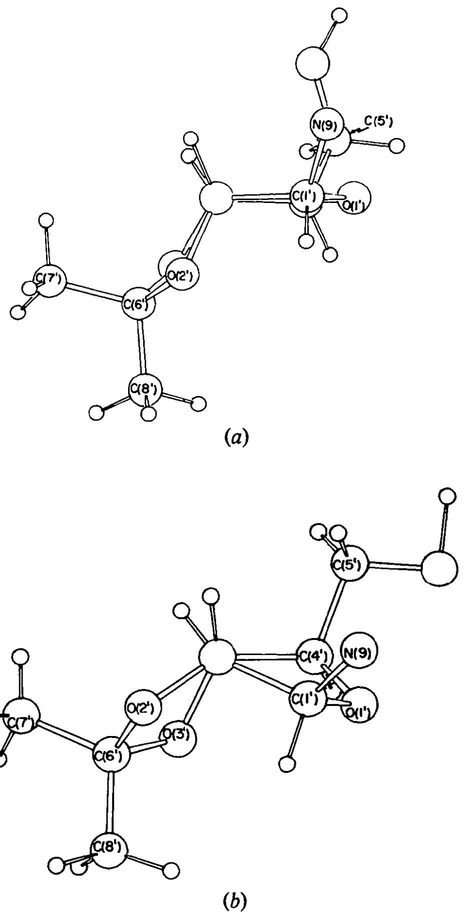

Fig. 3. View of the bicyclic group along the C(2′)—C(3′) bond. (*a*) Molecule *A*; (*b*) molecule *B*.

Geometry of the base

Corresponding dimensions in the purine rings of molecules *A* and *B* generally agree within 3σ; the greatest differences are localized within the imidazole moieties; the C(8)—N(9) bond lengths and the C(4)—N(9)—C(1′) bond angles differ by 0·028 Å and 1·8°, respectively. The values for the adenine bond lengths and angles of both molecules show a mean deviation of 0·013 Å and 0·6°, respectively, from those observed in well determined structures of neutral adenine nucleosides (Rao & Sundaralingam, 1970; Lai & Marsh, 1972; Rohrer & Sundaralingam, 1970; Bunick & Voet, 1974).

Planarity of the base

The least-squares planes through the nine atoms of the purine ring of molecules *A* and *B* are described by the equations $0.1913X + 0.9538Y + 0.2315Z = 7.4020$ and $0.1521X + 0.9578Y - 0.2438Z = 6.4632$ respectively, where *X*, *Y*, and *Z* are measured in Å along the crystallographic *a*, *b* and *c* axes. The C(1′) and N(6) atoms in molecule *A* show significant deviations of 0·083 and 0·022 Å, respectively, on opposite sides from this plane. The corresponding atoms in molecule *B* do not deviate significantly from the plane of the base. Both molecules *A* and *B* show a slight dihedral angle between the imidazole and pyrimidine least-squares planes of 1·1 and 0·7°, respectively. These are well within the normal values observed in similar systems (Sletten & Jensen, 1969).

Geometry of the fused furan-dioxolane group

The bicyclic moiety is comprised of the ribofuranose and dioxolane rings fused at the common C(2′) and C(3′) atoms. There are substantial conformational differences between the bicyclic systems of the two independent molecules, and these are reflected in the molecular geometry. The corresponding bond distances in the two independent molecules are in good agreement with each other and are also comparable with the average values for C(2′) and C(3′) *endo* sugars (Sundaralingam, 1973, 1975). However, the C(1′)—O(1′) bonds (1·366 Å, molecule *A*; 1·391 Å, molecule *B*), particularly that of molecule *A*, are shorter than those normally observed in the crystal structures of ribosides (1·412 Å). The unusually short C(1′)—O(1′) distance in molecule *A* suggests that the unpuckered (planar) conformation of the furanose ring enhances the double-bond character of this bond. Further aspects of the correlation between the length (double-bond character) of the C(1′)—O(1′) bond and the furanose and glycosyl conformations will be reported elsewhere (Sprang & Sundaralingam, 1978*b*).

The corresponding endocyclic bond angles within the furanose and dioxolane groups in molecules *A* and *B* differ significantly. The latter also deviate substantially from the values exhibited by normal C(2′) *endo* and C(3′) *endo* ribosides (Sundaralingam & Jensen, 1965; Saenger & Eckstein, 1970; Sundaralingam, 1965, 1973, 1975). It has been previously recognized that, as a general rule, the atom(s) most severely puckered with respect to the ribose plane undergoes contraction at the endocyclic bond angle (Sundaralingam, 1965). The ribose moiety of molecule *A* is essentially planar. Consequently, the endocyclic angles, particularly those about the C(2′) and C(3′) atoms, are greater than those of puckered ribosides and more nearly equal to each other. The endocyclic angle which seems most affected by the planar ring conformation (molecule *A*, 113·2°) compared to that in the puckered ribofuranose (molecule *B*, 109·4°), is that about the ribose ring oxygen O(1′).

The endocyclic angles of the ribofuranose ring of molecule *B* are likewise affected by cyclization and ring pucker. The angle at C(4′)*B*, 104·0°, is contracted as expected since the ribose assumes a C(3′) *exo*, C(4′) *endo* pucker. However, the endocyclic angle at C(3′)*B*, 105·3°, is greater than that observed in C(3′)-puckered sugars. The angle at C(2′)*B*, 102·4°, approaches the values observed in the ^2E and ^3E puckered sugars. The endocyclic angle at the C(1′)*B* atom is significantly greater than that in the C(2′) *endo* and C(3′) *endo* sugars and is almost ideally tetrahedral. It is noteworthy that the C(1′) atom is the farthest removed from the puckered C(3′)*B* and C(4′) atoms in the ribose ring, and consequently suffers the least contraction. The effects of the ring fusion at C(2′) and C(3′) are especially profound in the dioxolane ring endocyclic angles at C(2′) (103·5, 105·1°) and C(3′) (105·6, 101·7°) of both molecules *A* and *B*. These values are considerably less than in normal nucleosides (Sundaralingam, 1973, 1975). The endocyclic angles about the isopropylidene carbon atoms C(6′) are, as expected, significantly less (104·6, 104·8°) than the exocyclic angles (mean value: 110·4°).

The greatest degree of disparity in molecular geometry is exhibited in the C(3′)—C(4′)—C(5′) bond angle which is 116·8° in molecule *A* and 110·4° in molecule *B*. These values are within the normal range for nucleosides and are correlated with the torsion angles about the C(4′)—C(5′) bond and, to a lesser degree, the pucker of the furanose ring (Sprang, 1977).

Hydrogen bonding

The hydrogen-bonding configuration is described by a network of self-paired adenine moieties which form a sheet parallel to the *ac* plane (Fig. 4). The bases in the self pair are markedly twisted with respect to each other, forming a dihedral angle of 27·6°. This mode of pairing is observed twice in this structure, between molecules *A* and *B* and between *B′* and *A*, where *B′* is related to *B* by a unit translation along the *c* axis. Both Watson–Crick [N(6) and N(1)] and Hoogsteen [N(6) and N(7)] sites of the adenine moieties are involved (Table 5). The adenine pairing scheme observed in this structure has been observed in several other neutral adenine bases, nucleosides and nucleotides, *viz*. 9-ethyladenine (Kaneda & Tanaka, 1976), 9-methyladenine (Stewart & Jensen, 1964), deoxyadenosine (Watson, Sutor & Tollin, 1965), 2′-*O*-methyladenosine (Prusiner & Sundaralingam, 1976), and a platinum(II) complex of adenosine 5′-phosphate (Wong & Lippard, 1977). Average base-pairing geometries for this 'hybrid' pairing scheme have been tabulated and discussed by Prusiner & Sundaralingam (1976). It is found that the corresponding values for the IPLA pairs are well within these limits. In all of the above cases, the bases which participate in an individual pair are related by a crystallographic (one independent molecule in the asymmetric unit) or pseudo-screw axis (two independent molecules) passing through their respective amino N(6) nitrogen atoms. In all of the nucleosides which are engaged in this hydrogen-bonding scheme, the N(3) atom is hydrogen bonded to the O(5′) atom of a translation-related molecule, regardless of the conformation around the C(4′)—C(5′) bond (*gauche*$^+$ or *trans*). The C(4′)—C(5′)—O(5′)—H(O5′) torsion is invariably *trans*.

Molecular packing

Molecules *A* and *B* are related by a pseudo-screw axis in the plane of the base pairs. The mean and r.m.s. deviations between pairs of pseudo-screw related atoms in molecules *A* and *B* is 0·480 and 0·375 Å, respectively. The corresponding values obtained by fitting the atoms of the bases alone are 0·024 and 0·021 Å, respectively. The two molecules *A* and *B* (Fig. 4) are related by a rotation of 174·4° about, and a translation

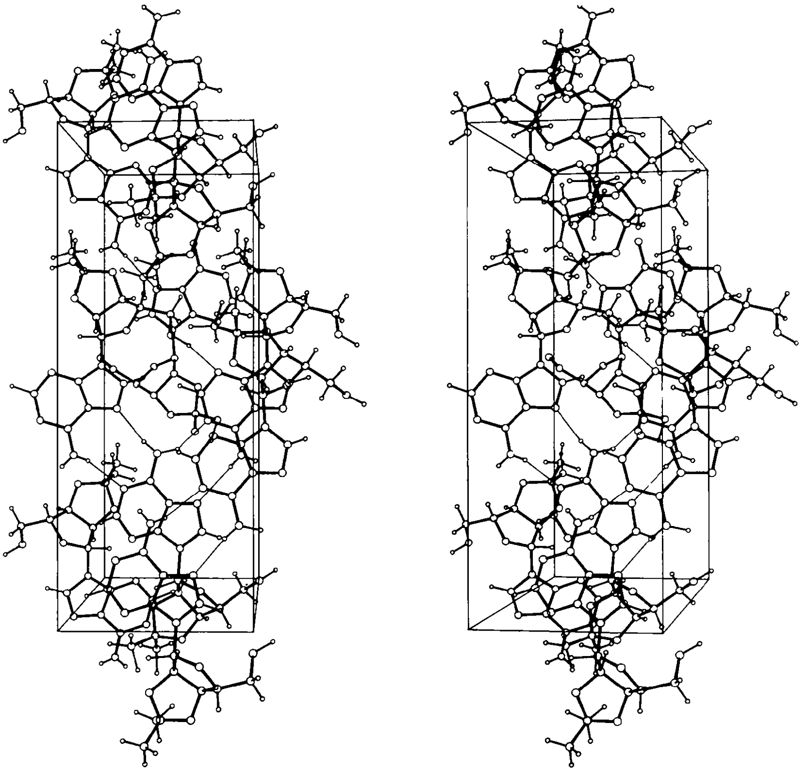

Fig. 4. Stereoview of the unit-cell contents shown approximately along the *b* axis.

Table 5. *Hydrogen-bond distances and angles and short contacts in 2′,3′-O-isopropylideneadenosine*

Bond *A*–H···*B*	Symmetry No. for *B**	Translation for *B* *x*	 *y*	 *z*	Distance (Å) *A*–H	 H···*B*	 *A*···*B*	Angle (°) *A*–H···*B*
N(6)*A*–H(6)1*A*···N(7)*B*	1	0	0	−1	0·77	2·34	3·097	169
N(6)*A*–H(6)2*A*···N(1)*B*	1	0	0	0	0·76	2·16	2·864	159
N(6)*B*–H(6)2*B*···N(7)*A*	1	0	0	0	0·91	2·42	3·046	171
N(6)*B*–H(6)1*B*···N(1)*A*	1	0	0	1	0·98	2·01	2·890	148
O(5′)*A*–H(O5′)*A*···N(3)*A*	1	0	0	1	1·01	1·89	2·881	167
O(5′)*B*–H(O5′)*B*···N(3)*B*	1	0	0	1	1·13	1·88	2·868	155

Table 5 (*cont.*)

Short contacts (Å)

Contact *A*···*B*	Symmetry No. for *B**	Translation for *B* *x*	 *y*	 *z*	Distance *A*···*B*
O(5′)*A*···C(2)*A*	1	0	0	1	3·205
C(2)*A*···O(5′)*B*	2	0	1	−2	3·017
N(1)*A*···O(5′)*B*	2	0	1	−2	3·239
C(8)*A*···O(1′)*B*	2	0	1	−1	3·315
N(7)*A*···O(1′)*B*	2	0	1	−1	3·211
C(5)*A*···O(1′)*B*	2	0	1	−1	3·280

* Symmetry No. (1) x,y,z; (2) $\frac{1}{2}-x, -y, \frac{1}{2}+z$.

of 4·12 Å along, a line which passes through the point (6·34, 6·96, 0·28 Å) and makes angles of 88·0, 87·5 and 3·2° with respect to the *a*, *b* and *c* axes of the unit cell. Degeneration from an ideal screw relationship arises as a consequence of the differing conformations of the sugar moieties and the slight differences in the base-pairing geometries (Table 5).

There are short non-bonded contacts between the O(1′) ribose-ring oxygen of molecule *B* and the imidazole atoms of the molecule *A* below. Interactions of this type are quite prevalent among nucleoside and nucleotide crystal structures (Bugg, Thomas, Sundaralingam & Rao, 1971). Other stacking interactions involving the bases appear to be weak. The amino nitrogen atom of molecule *A* overlaps the pyrimidine ring of molecule *B* and makes contacts of 3·500 and 3·622 Å with the atoms C(4)*B* and C(5)*B*, respectively. The methyl groups are clustered, but there are no contacts between methyl carbon atoms of less than 3·5 Å.

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